REMARKS

Claims 24 and 30 have been amended to more correctly specify that the domains are with respect to the proteins and not the gene. Claims 24 and 30 have further been amended to specify that the cell death domain of the Cmv2b protein is an inactive cell death domain. Finally, claims 24 and 30 have been amended to specify that the Tav2b protein is encoded by nucleotides 20-304 of SEQ ID NO:1 and that the Cmv2b protein is encoded by nucleotides 6-305 of SEQ ID NO:4. Support for the coding sequences of the Tav2b and Cmb2b proteins is found in the original Sequence Listing in view of the disclosure and Figure 3 showing the length of the native proteins.

Claims 26 and 32 have been amended to be consistent with the amended language of claims 24 and 30.

Claim 33 has been amended to correct a typographical error.

Claim 38 has been amended to provide proper antecedent basis.

It is submitted that none of the above amendments constitute new matter, and their entry is requested.

The Examiner has rejected claims 24, 26, 30 and 32-43 under U.S.C. § 112, second paragraph for being indefinite. It is submitted that the amendment to the claims to specify the cell death domain of the Cmv2b protein is inactive obviates this indefiniteness rejection. Withdrawal of this rejection is requested.

The Examiner has rejected claims 24, 26, 30 and 32-43 under U.S.C. § 112, first paragraph for lack of written description. In her rejection, the Examiner contends that the gene sequence should be set forth in the claims. Although Applicant submits that the specification fully describes the genes so that a skilled artisan recognizes that he was in possession of the invention at the filing date of the present invention, claims 24 and 30 have nevertheless been amended to include reference to the coding sequences for the Tav2b and Cmv2b genes in order to expedite the prosecution of this application. It is submitted that the amendment of the claims to specify these sequences obviates this written description rejection. Withdrawal of this rejection is requested.

The Examiner has rejected claims 24, 26, 30 and 32-43 under 35 U.S.C. § 112, first paragraph for lack of enablement based on a lack of written description. Since the amended claims comply with the written description requirement as described above, it is submitted that this basis of rejection is no longer applicable. Withdrawal of this rejection is requested.

The Examiner has rejected claims 24, 26, 30 and 32-43 under 35 U.S.C. § 112, first paragraph for lack of enablement. It is submitted that the Examiner is in error in this rejection.

Applicant initially notes that the claims are directed to two classes. First, claims 24, 26, 37, 42 and 43 are to a transgenic plant that has been transformed with a DNA sequence that encodes a protein comprising two domains. Claims 35 and 40 are directed to a seed of the transgenic plant. Claims 36 and 41 are directed to a propagule of the transgenic plant. The two domains of the protein are an N-terminal resistance domain and a C-terminal inactive cell death domain. The N-terminal resistance domain is the resistance domain of the Tav2b protein. The C-terminal inactive cell death domain is selected from the group consisting of an inactive cell death domain of the Tav2b protein and the inactive cell death domain of the Cmv2b protein. The Tav2b protein is encoded by nucleotides 20-304 of SEQ ID NO:1. The Cmv2b protein is encoded by nucleotides 6-305 of SEQ ID NO:4. The DNA sequence encoding the two domain protein is operatively linked to a promoter that is capable of causing expression of the DNA sequence in the plant when infected with a pathogenic organism.

Second, claims 30, 32-34, 38 and 39 are directed to an expression vector comprising a DNA sequence that encodes a protein comprising two domains. The two domains of the protein are an N-terminal resistance domain and a C-terminal inactive cell death domain. The N-terminal resistance domain is the resistance domain of the Tav2b protein. The C-terminal inactive cell death domain is selected from the group consisting of an inactive cell death domain of the Tav2b protein and the inactive cell death domain of the Cmv2b protein. The Tav2b protein is encoded by nucleotides 20-304 of SEQ ID NO:1. The Cmv2b protein is encoded by nucleotides 6-305 of SEQ ID NO:4. The DNA sequence encoding the two domain protein is operatively linked to a plant-active promoter.

Applicant submits that the Examiner's arguments made with respect to her rejection for lack of enablement do not apply equally to both of these classes. For example, the fact that tobacco has been transformed with the claimed expression vector and the two domain protein has been expressed in tobacco is sufficient to demonstrate enablement for the expression vector. Also, plant active promoters are well known in the art. A skilled artisan knows that promoters are selected on the basis of the host and are selected to be operable in the host. This knowledge has existed in the art since the beginning of genetic engineering and is nothing new. For example, one well known plant active promoter is the 35S promoter of cauliflower mosaic virus. Another well known plant active promoter is the NOS promoter. Thus, a skilled artisan can readily select a plant active promoter for use with a desired host plant. In addition, the references provided with the previous Amendment demonstrates that a plant pathogen activated promoter controls the expression of a chimeric gene. See, the abstracts by Beilmann et al. (1992), Eyal et al. (1993), Hennig et al. (1993), Shah and Klessig (1996), Shah et al. (1997), Tornero et al. (1997) and Warner et al. (1993). Thus, a skilled artisan would reasonably expect that the expression vector comprising a two-domain gene under control of a plant pathogen activated promoter would be capable of expressing the two-domain protein. As demonstrated by these references, Applicant submits that this feature of the invention is neither unpredictable or requires any undue experimentation. Furthermore, Applicant submits that the Examiner has not offered any scientific reasoning or basis to rebut the teachings of these references and thus the enablement of the claims directed to the expression vector. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir.1993); *In re Marzocchi*, 169 USPQ 367 (CCPA 1973). Accordingly it is submitted that Applicant has demonstrated how to make and use the claimed expression vector. That is all that is required by 35 U.S.C. § 112, first paragraph. Thus, Applicant submits that the expression vector of claims 30, 32-34, 38 and 39 is fully enabled by the specification. Withdrawal of the enablement rejection with respect to claims 30, 32-34, 38 and 39 is requested.

Applicant further submits that the Examiner's analysis of the Wands factors, when properly considered, does not support an enablement rejection of the claims directed to transgenic plants or its seeds or propagules. The proper analysis of the Wands factors follows.

The breadth of the claims and the nature of the invention.

Claims 24, 26, 37, 42 and 43 are directed to a transgenic plant and its seed or propagule that is stably transformed with a DNA sequence encoding a protein that comprises two domains. The two domains of the protein are narrowly defined with respect to what the domains are and the DNA sequence that encodes them. The DNA sequence is linked to a promoter that is capable of causing expression of the DNA sequence when the transgenic plant is infected with a pathogen.

The predictability or lack thereof in the art.

The Examiner contends that it is unpredictable as to the results of infecting a given plant with a given plant pathogen relying on Agrios (*Plant Pathology*, 3rd Ed., Academic Press, San Diego, p. 43, 1988). However, the host range of a particular plant pathogen was well known in the art at the time of the present invention. Both the natural host range and experimental host range of plant viruses have been well documented. For example, tobacco mosaic virus is known to naturally infect *Nicotiana tabacum* and is found in many other plant species. Tobacco mosaic virus is also known to be able to experimentally infect *Beta vulgaris*, *Capsicum frutescens*, *Chenopodium amaranticolor*, *Chenopodium hybridum*, *Chenopodium quinoa*, *Cucumis melo*, *Cucumis sativus*, *Cucurbita pepo*, *Datura stramonium*, *Lactuca sativa*, *Lycopersicon esculentum*, *Lycopersicon pimpinellifolium*, *Nicotiana benthamiana*, *Nicotiana bigelovii*, *Nicotiana clevelandii*, *Nicotiana debneyi*, *Nicotiana glutinosa*, *Nicotiana rustica*, *Nicotiana sylvestris*, *Nicotiana tabacum*, *Papaver nudicaule*, *Phaseolus vulgaris*, *Physalis floridana*, *Physalis peruviana*, and *Solanum tuberosum*. The natural and experimental host range of plant viruses was known in the art prior to the filing date of the present application. For example, this knowledge was available in: *Virus Taxonomy: The Classification and Nomenclature of Viruses. The Sixth Report of the International Committee on Taxonomy of Viruses*,

F.A. Murphy, F.A. et al., eds., Springer-Verlag, Vienna, 1995. This information was also published in *Archives of Virology* , Supplement 10, 1-586, 1995.

Similarly, the host range of other plant pathogens, such as fungi were well known at the time of the present invention. For example, fungal species, their plant hosts and host-fungus combinations are described in Farr, D.F. et al., *Fungi on Plants and Plant Products in the United States* (FOPP), APS Press, St. Paul, Minnesota, 1989. In addition, fungus and host interactions can be found in *Ainsworth & Bisby's Dictionary of Fungi*, Hawksworth et al., eds, Eighth ed., CAB International. Wallingford, Oxon, U. K., 1995. Bacteria and their host plants are described in *Pathogenesis & Host Specificity in Plant Diseases, Histopathological, Biochemical, Genetic and Molecular Bases*, Singh, U.S. et al., eds., Pergamon Press, Oxford, 1996. This latter reference also includes information with respect to plant pathogenic viruses and fungi. Applicants note that each of the above cited references describing plant-pathogen interactions are all more recent than the cited Agrios reference. These references clearly describe the knowledge in the art, knowledge that does not need to be set forth in the specification (*see* M.P.E.P. § 2164.05(a)), concerning interactions and host ranges of plant pathogens. Thus, Applicant submits that a skilled artisan knows the interactions between plants and their pathogens. In view of this knowledge, a skilled artisan could predictably select the appropriate pathogen for a particular plant species. Thus, Applicant submits that the art is predictable as to the specific interaction between a given pathogen and a given plant species.

Applicants also submit that the selection of a promoter to use in transgenic plants is not unpredictable. Any promoter from those pathogens known to infect a given plant can be used as readily known by a skilled artisan at the time of the present invention. Furthermore, Applicant submits that plant pathogen activated promoters were also well known at the time of the present invention and were known to predictably control expression of a gene under their control in transgenic plants. This knowledge of plant pathogen activated promoters and their use in expressing genes in transgenic plants is shown in the references submitted with the previous Amendment. Specifically, the abstracts by Beilmann et al. (1992), Eyal et al. (1993), Hennig et al. (1993), Shah

and Klessig (1996), Shah et al. (1997), Tornero et al. (1997) and Warner et al. (1993) demonstrate that a plant pathogen activated promoter controls the expression of a chimeric gene in transgenic plants. Thus, a skilled artisan would reasonably expect that a two-domain gene under control of a plant pathogen activated promoter would be expressed in a transgenic plant. As demonstrated by these references, Applicant submits that this feature of the invention, i.e., plant pathogen activated promoter, is neither unpredictable or requires any undue experimentation. Furthermore, Applicant submits that the Examiner has not offered any scientific reasoning or basis to rebut the teachings of these references and thus the enablement of the claims directed to transgenic plants, seeds or propagules containing a two-domain gene under control of a promoter that is capable of causing expression of the gene when the plant is infected with a pathogenic organism, and particularly where the promoter is a plant pathogen activated promoter. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir.1993); *In re Marzocchi*, 169 USPQ 367 (CCPA 1973). Thus, Applicant submits that there is no unreasonable predictability with respect to using plant pathogen activated promoters to control the expression of the two-domain gene. Consequently, the nature of the invention is predictable to a skilled artisan and thus fully enabled by the specification.

Amount of guidance and the presence of working examples or lack of working examples.

In this portion of the analysis, the Examiner essentially contends that the claims are not enabled because a working example is not provided showing the expression of a two-domain gene under the control of a plant pathogen activated promoter. First, Applicant notes that, contrary to the statement by the Examiner, the specification does include a teaching of a two-domain gene under control of a plant pathogen activated promoter. This aspect of the invention is taught at page 13, line 33 - page 14, line 6. It is true that there is no working example of such a construct or a transgenic plant containing the construct. However, that fact does not mean that the specification does not teach the construct or a transgenic plant containing the construct. As shown by the cited passage from the specification, the specification provides guidance for a construct comprising a plant pathogen activated promoter and a two-domain gene. Guidance is all that is required – there is no

requirement for working examples. In fact, as demonstrated above, it was well known that plant pathogen activated promoters were capable of controlling the expression of genes in transgenic plants. Applicant has provided objective enablement of a two-domain gene under control of a plant pathogen activated promoter that is predictable from the knowledge in the art. The Examiner has not provided any basis for doubting this objective enablement or the teachings in the art concerning the expression of genes under control of a plant pathogen activated promoter. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir.1993); *In re Marzocchi*, 169 USPQ 367 (CCPA 1973).

Amount of experimentation necessary.

Contrary to the Examiner's assertion, no undue trial and error would be required to practice the claimed invention. As detailed above, it was well known in the art at the filing date of the present application the specific interactions between plant pathogens and plant species, including the host range, both natural infection and experimental infection, of plant pathogens. Thus, there would be no undue trial and error to select a particular pathogen for a given plant species in view of this knowledge by a skilled artisan. The Examiner has not provided any sound scientific reason or basis to rebut this knowledge in the art concerning plant-pathogen interactions. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir.1993); *In re Marzocchi*, 169 USPQ 367 (CCPA 1973).

In this portion of the rejection, the Examiner interspersed several questions which are readily answered by reference to the specification and the claims. For example, the Examiner asks to what the resistance is for the N-terminal resistance domain of the Tav2b gene. This resistance is shown in the specification at page 11, line 25 - page 12, line 14. According to this passage, the resistance is resistance activation. The resistance activation is first to tomato aspermy virus (which is how the domain was identified), and second to pathogens in general as a result of the systemic acquired resistance (SAR) effect as well known in the art, as shown by the Bowling et al. (1994) and Ryals et al. (1996) articles provided with the previous Amendment. With respect to the Tav2b and Cmv2b genes, Applicant notes that the coding sequence of these genes are set forth in SEQ ID NOs:1 and 4, respectively, as described in the specification, and as now set forth in the amended claims. The

specification teaches that the "inactive" domain is not capable of generating a cell death response as opposed to the "active" domain which is capable of generating a cell death response. See, page 12, lines 15-33. All of these features are clearly disclosed and described in the specification and are readily recognized by a skilled artisan upon reading the specification.

In addition, as previously described, plant active promoters were well known in the art at the time the present application was filed. Similarly, plant pathogen activated promoters were also well known in the art at the time the present application was filed. The choice of a particular promoter for a specific plant species based on the chosen host was well known at the filing date of the present application. The Examiner has not provided any scientific evidence or basis to establish that known plant active promoters could not be used to control the expression of the two-domain gene, especially in view of the knowledge in the art that such promoters naturally function as guided by the specification. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir.1993); *In re Marzocchi*, 169 USPQ 367 (CCPA 1973). No myriad of experimentation is necessary to select and use well know plant active promoters.

Applicant has provided guidance in the specification concerning the expression of a two-domain gene in transgenic plants and the subsequent resistance and SAR response. Applicant has provided working examples demonstrating the expression of a two-domain gene in multiple transgenic plant species. Applicant has provided working examples of expression of a two-domain gene under control of a plant active promoter. Applicant has provided guidance in the specification for the use of plant pathogen activated promoters to control the expression of a two-domain gene. Applicant has demonstrated that skilled artisans knew that plant pathogen activated promoters were useful for controlling expression of genes in transgenic plants and that gene expression was controlled by such promoters. The Examiner has not provided any evidence to the contrary with respect to this demonstration of knowledge in the art. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir.1993); *In re Marzocchi*, 169 USPQ 367 (CCPA 1973). Applicant has provided guidance in the specification that resistance to other plant pathogens is generated in response to resistance domain

of the two-domain protein in view of the SAR effect. This effect is described at page 2, line 29 - page 3, line 21. The SAR effect was well known in the art at the filing date of the present application. See, the Bowling et al. (1994) and Ryals et al. (1996) articles. It was known that the resistance effect caused by resistance to one pathogen is applicable to other pathogens that infect that particular plant species in which the resistance effect was generated.

It has been demonstrated that plant active promoters were known and that plant pathogen activated promoters were known at the filing date of the present application. It has further been demonstrated that it was known that plant active promoters and plant pathogen activated promoters were known to control the expression of genes under their control. On the basis of this knowledge in the art and the predictability in the art, a skilled artisan would have reasonable expectation that a two-domain gene as claimed under control of a plant active promoter of a plant pathogen activated promoter would be expressed in a transgenic plant (or by an expression vector). The Examiner has not provided any scientific evidence or basis to rebut this knowledge and expectation by a skilled artisan. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir.1993); *In re Marzocchi*, 169 USPQ 367 (CCPA 1973).

In summary, Applicant has provided sufficient guidance, in combination with the working examples, to enable a skilled artisan to make and use an expression vector and a transgenic plant that contain a two-domain gene under control of a plant active promoter or a plant pathogen activated promoter. The claims specify the two-domain gene on the basis of the resistance domain of the Tav2b protein and an inactive cell death domain of either the Tav2b protein or the Cmv2b protien in which the Tav2b protein or the Cmv2b protein are encoded by the coding sequences of SEQ ID NOs:1 and 4, respectively. The use of plant active promoters and plant pathogen activated promoters were well known in the art and well known to be useful for generating expression vectors and transgenic plants for the expression of genes under their control. Such use was predictable and reasonably expected by a skilled artisan. The Examiner has not presented any scientific evidence to rebut this predictability. The host range of plant pathogens was known at the filing date of the

present application. Thus, it was predictable as to what plant a particular plant pathogen would infect. The Examiner has not presented any scientific evidence to rebut this knowledge and predictability in the art concerning the known host range of plant pathogens. Accordingly, the specification has provided sufficient guidance that addresses all of the issues noted by the Examiner, and thus fully enables the claimed invention. Thus, Applicant submits that the transgenic plant, seed and propagule of claims 24, 26, 37, 42 and 43 are fully enabled by the specification. Applicant further submits that the expression vector of claims 30, 32-34, 38 and 39 is fully enabled by the specification.

In view of the above amendments and remarks, it is submitted that the specification fully enables the claimed subject matter in accordance with the requirement of 35 U.S.C. § 112, first paragraph. Withdrawal of this rejection is requested.

In view of the above amendments and remarks, it is submitted that the claims satisfy the requirements of the patent statutes and are patentable over the prior art. Reconsideration of the instant application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

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